



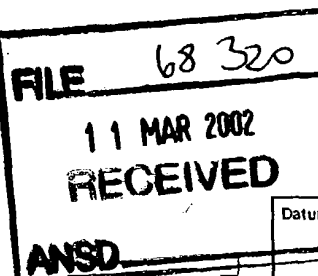
P.B. 5818 - Patentamt
2280 HV Rijswijk (ZH)
☎ (070) 340 2040
Tx 31651 epo nl
FAX (070) 340 3016

Europäisches
Patentamt
Zweigstelle in
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European
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Search
Division

Office européen
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Département à
La Haye
Division de la
recherche

Dzieglewska, Hanna Eva
Frank B. Dehn & Co.,
European Patent Attorneys,
179 Queen Victoria Street
London EC4V 4EL
GRANDE BRETAGNE



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Anmelder/Applicant/Demandeur//Patentinhaber/Proprietor/Titulaire THE GENERAL HOSPITAL CORPORATION	

COMMUNICATION

The European Patent Office herewith transmits the partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,-) or the equivalent applicable on the date of payment is payable.

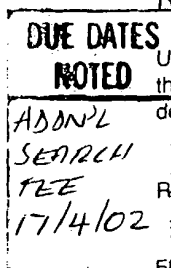
This applies also to the search fees requested under Rule 46(1) EPC.

See also OJ EPO 06/1999, 405.

- ☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.
- ☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.



Note to users of the automatic debiting procedure:



Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER

EPO Form 1507.2 (07.99)



PARTIAL EUROPEAN SEARCH REPORT

Application Number

under Rule 46, paragraph 1 of the European Patent EP 96 94 0523 Convention

1



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	HERMANT DANIEL ET AL: "Functional conservation of the Salmonella and Shigella effectors of entry into epithelial cells." MOLECULAR MICROBIOLOGY, vol. 17, no. 4, 1995, pages 781-789, XP001055768 ISSN: 0950-382X	1-7	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
Y	*Abstract; page 782, right hand column, last full paragraph - page 786, left hand column, first full paragraph and figure 2* & DATABASE EMBL 'Online! Accession Number x82670, 4 October 1995 (1995-10-04) HERMANT D ET AL: "Functional conservation of the Salmonella and Shigella effectors of entry into epithelial cells." *99,2% identity with SEQ ID NO:1, 99,6% identity with SEQ ID NO:2, 89,9% identity with SEQ ID NO:3, 97,9% identity with SEQ ID NO:4 and 96,4% identity with SEQ ID NO:15*	9-11	
Y	PEGUES DAVID A ET AL: "PhoP/PhoQ transcriptional repression of Salmonella typhimurium invasion genes: Evidence for a role in protein secretion." MOLECULAR MICROBIOLOGY, vol. 17, no. 1, 1995, pages 169-181, XP001034139 ISSN: 0950-382X *Abstract and Discussion*	9-11	



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: claims 1-5, 8-14 and 16-20 (partially)

Invention 1 concerns a DNA having the nucleotide sequence SEQ ID NO:1 and encoding a Salmonella secreted protein (SspB) having the amino acid sequence SEQ ID NO:5. This invention further concerns a cell containing said DNA, an antibody which binds said SspB protein, methods of detecting the presence of Salmonella in a mammal or in a biological sample, the use of said SspB protein for the preparation of a Ssp chimeric antigenic, the use of a bacterial cell in which the expression of said DNA is increased/decreased for the preparation of a composition and a vaccine comprising a bacterial cell with attenuated virulence due to decrease secretion of said SspB.

2. Claims: claims 1-20 (partially)

Invention 2 concerns a DNA having the nucleotide sequence SEQ ID NO:2 and encoding a Salmonella secreted protein (SspC) having the amino acid sequence SEQ ID NO:6. This invention further concerns a cell containing said DNA, an antibody which binds said SspC protein, methods of detecting the presence of Salmonella in a mammal or in a biological sample, the use of said SspC protein for the preparation of a Ssp chimeric antigenic, the use of a bacterial cell in which the expression of said DNA is increased/decreased for the preparation of a composition and a vaccine comprising a bacterial cell with attenuated virulence due to decrease secretion of said SspC.

3. Claims: claims 1-20 (partially)

Invention 3 concerns a DNA having the nucleotide sequence SEQ ID NO:3 and encoding a Salmonella secreted protein (SspD) having the amino acid sequence SEQ ID NO:7. This invention further concerns a cell containing said DNA, an antibody which binds said SspD protein, methods of detecting the presence of Salmonella in a mammal or in a biological sample, the use of said SspD protein for the preparation of a Ssp chimeric antigenic, the use of a bacterial cell in which the expression of said DNA is increased/decreased for the preparation of a composition and a vaccine comprising a bacterial cell with attenuated virulence due to decrease secretion of said SspD.



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

4. Claims: claims 1-5, 8-14 and 16-20 (partially)

Invention 4 concerns a DNA having the nucleotide sequence SEQ ID NO:4 and encoding a Salmonella secreted protein (SspA) having the amino acid sequence SEQ ID NO:8. This invention further concerns a cell containing said DNA, an antibody which binds said SspA protein, methods of detecting the presence of Salmonella in a mammal or in a biological sample, the use of said SspA protein for the preparation of a Ssp chimeric antigenic, the use of a bacterial cell in which the expression of said DNA is increased/decreased for the preparation of a composition and a vaccine comprising a bacterial cell with attenuated virulence due to decrease secretion of said SspA.

5. Claims: claims 1-3, 5-14 and 16-20 (partially)

Invention 5 concerns a DNA having the nucleotide sequence SEQ ID NO:13 and encoding a Salmonella secreted protein (SspH) having the amino acid sequence SEQ ID NO:14. This invention further concerns a cell containing said DNA, an antibody which binds said SspH protein, methods of detecting the presence of Salmonella in a mammal or in a biological sample, the use of said SspH protein for the preparation of a Ssp chimeric antigenic, the use of a bacterial cell in which the expression of said DNA is increased/decreased for the preparation of a composition and a vaccine comprising a bacterial cell with attenuated virulence due to decrease secretion of said SspH.

6. Claims: claim 21 (completely) and claims 1-3, 5, 6, 8-14 and 16-20 (partially)

Invention 6 concerns a DNA having the nucleotide sequence SEQ ID NO:10 and encoding a Salmonella secreted protein with tyrosine phosphatase activity (StpA) having the amino acid sequence SEQ ID NO:12. This invention further concerns a cell containing said DNA, an antibody which binds said StpA protein, methods of detecting the presence of Salmonella in a mammal or in a biological sample, the use of said StpA protein for the preparation of a Ssp chimeric antigenic, the use of a bacterial cell in which the expression of said DNA is increased/decreased for the preparation of a composition and a vaccine comprising a bacterial cell with attenuated virulence due to decrease secretion of said StpA. This



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

invention further comprises a method of dephosphorylating a protein.

7. Claim : claims 6 and 7 (partially)

Invention 7 concerns a polypeptide (IagB) having the amino acid sequence SEQ ID NO:11 and being encoded by a nucleic acid having the nucleotide sequence SEQ ID NO: 9.

Motivation of lack of unity

The present application does not comply with the requirements of unity of invention (Article 82 EPC and Rule 30 EPC).

Seven separate inventions have been identified. Each of them is characterised by an individual "special technical feature"; there is no technical interrelation between these inventions (see below).

Regarding that the search of inventions 2-4 does not require a considerable additional amount of work, the Partial Search Report has been established for inventions 1-4, i.e. the subject-matter relating to proteins SspB, SspC, SspD and SspA.

The applicants are therefore asked to pay three additional search fees. Otherwise the European Search Report will be limited to inventions 1-4 as specified above (Rule 46(1) EPC).

The following arguments reflect the opinion of the Search Division concerning unity of invention:

Rule 30(1) EPC demands that "Article 82 EPC shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding "special technical features". The expression "special technical features" shall mean those technical features which define a contribution which each of the claimed inventions considered as a whole makes over the prior art".

The presently claimed subject-matter does not fulfill the necessary requirements on unity of invention as outlined above:



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1). Inventions 1-6 and Invention 7 do not share such a "special technical feature"
(non unity objection motivated "a priori")

Inventions 1-6 and Invention 7 are drafted to two different problems, which are solved with independent solutions.

- The problem of inventions 1-6 is the provision of Salmonella secreted proteins. The problem is solved with proteins having amino acid sequences SEQ ID NOs: 5, 6, 7, 8, 12 and 14.
- The problem of invention 7 is the provision of a polypeptide. The problem is solved with a polypeptide having an amino acid sequence SEQ ID NO: 11.

2). Inventions 1-6 do not share such a "special technical feature"
(non-unity objection motivated "a posteriori")

The technical relationship among the present subject-matter of Inventions 1-6 is that they all relate to Salmonella secreted proteins. However, this relation cannot be accepted to consist of a "special technical feature" as defined above, since it does not define a contribution which each of the different claimed inventions, considered as a whole, makes over the prior art.

In fact, Salmonella secreted proteins are known in the prior art. See for example:

- Molecular Microbiology, Vol. 18, No. 3, 1995, pages 479-490, (document cited in the IPER), discloses Salmonella typhimurium secreted proteins SspB, SspC, SspD and SspA (see abstract);
- Journal of Bacteriology, Vol. 177, No. 14, 1995, pages 3965-3971, discloses Salmonella secreted proteins SipB and SipC (see abstract);

In light of the above, the general inventive concept of Salmonella secreted proteins cannot be accepted to be novel over the prior art. Thus, Inventions 1-6 lack unity of invention because it is considered that each of the alleged inventions as listed above, has an individual and technically independent characteristic feature. Said alleged inventions are not so linked as to form a single general inventive concept.

Therefore, the problem underlying Inventions 1-6 can be defined as the provision of further Salmonella secreted proteins. The proteins defined by inventions 1-6 are different solutions to this problem.